Heritage Information Systems, Inc.

Clinical Edit Criteria Proposal

Drug/Drug Class: **Cipro XR® (Ciprofloxacin extended release)/Anti-infective Agent**

Prepared for:
Prepared by: Heritage Information Systems, Inc.

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose: The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis, apply clinical edit or require prior authorization for use.

Dosage Forms & Manufacturer: Each nearly white to slightly yellowish, filmcoated oblong-shaped tablet contains ciprofloxacin 500 mg/ BayerCorporation, West Haven, CT 06516

Summary of Findings: It is recommended that Cipro XR® be placed on clinical edit status and classified as a Non-Preferred Agent.

Status Recommendation:
- ☐ Prior Authorization (PA) Required
- ☐ Open Access
- ☒ Clinical Edit

Type of PA Criteria:
- ☐ Increased Risk of ADE
- ☒ Non-Preferred Agent
- ☐ Appropriate Indications
- ☐ PA Not Required

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis, apply clinical edit or require prior authorization for use. While prescription expenditures are increasing at double-digit rates, payors are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement o f qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction[1-4]

The choice of an antimicrobial agent for the treatment of an uncomplicated urinary tract infection (UTI) should be based on good absorption, good tolerability, and have as narrow a spectrum of activity as possible given the suspected pathogen(s). For acute uncomplicated cystitis, the most common form of UTI, the most frequently implicated microorganism is *Escherchiia coli*; the pathogens *Klebsiella pneumoniae* and *Proteus mirabilis* are found less frequently. Although traditional therapies have been 7 to 14 days in length, there are enough accumulated data to support single dose and 3 day regimens. The shorter regimens promote compliance, have a lesser risk of side effects, have less potential for development of resistance, and can be less expensive. Patients who should not receive shorter regimens include males, those with complicated UTIs, and those who have had previous infections with resistant bacteria.

Two double-strength tablets of Bactrim® is the most effective of the one-dose regimens. For the 3 day regimens, trimethoprim-sulfamethsoxazole (1 double-strength tablet twice daily for 3 days) is probably the least expensive choice. All of the marketed fluoroquinolones are approved for 3 day uncomplicated UTI regimens. While certainly effective therapy, some argue that fluoroquinolone therapy for uncomplicated UTIs is unnecessary, since the extra coverage they provide (eg., for *Pseudomonas aeruginosa*) is not needed for the average uncomplicated UTI. These agents may be particularly useful, however, in those parts of the country where 10-20% of *E. coli* strains are resistant to Bactrim® or for those with allergies to Bactrim® and other sulfa drugs.

Cipro XR® is an extended release version of Cipro®, the fluoroquinolone ciprofloxacin that has been marketed since the late 1980s. Cipro®, an immediate release product, is given twice daily. The new Cipro XR® can be used once daily. Of note, the patent for Cipro® expires in 2003; the generic version of Cipro® is expected in the second quarter of this year.

Dosage Form(s)[1]

Each nearly white to slightly yellowish, film coated oblong-shaped tablet contains:

- Ciprofloxacin……500 mg

Manufacturer[1]

Manufactured by: Bayer Corporation, West Haven, CT 06516

Indication(s) [1]

Cipro XR® is indicated for the treatment of uncomplicated urinary tract infections (acute cystitis) caused by the susceptible strains of the following microorganisms; *Escherichia coli*, *Proteus mirabilis*, *Enterococcus faecalis*, or *Staphylococcus saprophyticus*.

Clinical Efficacy[1] (mechanism of action/pharmacology, comparative efficacy)

Cipro XR® was compared to Cipro® (ciprofloxacin immediate-release tablets) in a randomized, double-blind, controlled clinical trial evaluating 905 patients with acute cystitis. Cipro XR® 500 mg once daily was compared to Cipro® 250 mg given twice daily, both given for three days. Both the clinical success and bacterial eradication rates were similar between the two treatment groups.

Adverse Effects[1]

In the clinical study discussed above, nausea (3%) and headache (2%) were reported more frequently in the Cipro XR®-treated patients.

Other reported adverse effects included abdominal pain, photosensitivity reactions, migraine, anorexia, constipation, diarrhea, dyspepsia, depersonalization, dizziness, maculopapular rash, pruritus, and taste perversion.

Drug Interactions[1]

Cipro XR® should be taken at least 2 hours before or 6 hours after antacids containing magnesium or aluminum, products containing iron, products containing zinc, and Videx® (didanosine) chewable/buffered tablets or pediatric powder.

When given together, Cipro XR® may increase serum concentrations of theophylline or increase its elimination half-life. Cipro XR® may reduce clearance of caffeine and prolong its elimination half-life.

Other potential drug interactions include hypoglycemia when Cipro XR® is used with glyburide, transient elevation in serum creatinine when Cipro XR® is used with cyclosporine, enhanced effects of warfarin when taken with Cipro XR®, and decreased renal tubular secretion of Cipro XR® when used with probenecid.

Dosage and Administration[1]

Uncomplicated Urinary Tract Infections (Acute cystitis):

- One tablet daily for 3 days

Tablets should not be split, crushed, or chewed. They are not interchangeable with immediate release Cipro®.

Use in Other Populations[1]

Pregnancy: Pregnancy Category C.

Nursing Mothers: Cipro XR® is excreted into the milk. Caution should be exercised when Cipro XR® is administered to a nursing woman.

Pediatric Use: Use of Cipro XR® in patients younger than 18 years has not been established.

Geriatric Use: No difference in the safety and effectiveness of immediate-release Cipro® in older patients versus younger patients were observed in clinical studies.

Cost Comparison [5] (at commonly used dosages)

The AWP of Cipro XR® is $8.66 per tablet. For the dose of one tablet daily, the cost for 3-day therapy is $25.99. In comparison, Cipro® 250 mg immediate release tablets cost $4.48 per tablet. For the dose of one tablet (250 mg) twice daily, the cost for 3 day therapy is $26.88.

Conclusion

Cipro XR® is an extended release version of Cipro®, the immediate release fluoroquinolone ciprofloxacin that has been marketed since the late 1980s. The generic version of Cipro® should be available in the second quarter of 2003.

Cipro XR® is indicated for once daily 3-day treatment of uncomplicated urinary tract infections (acute cystitis). When compared to 3-day therapy with twice daily immediate release Cipro®, Cipro XR® had similar bacteriologic and clinical efficacy, and was not as well tolerated.

Cipro XR® offers no advantage over older therapies.

Recommendation(s)

It is recommended that Cipro XR® be placed on clinical edit status.

Approval Criteria

- Diagnosis of uncomplicated urinary tract infection
- Therapy limitation – 3 days

Denial Criteria

- Patients age less than 18 years
- Therapy exceeding 3 days of treatment

References

1. Cipro XR® package insert. Bayer Corporation; December 2002.
2. Short RM, Burnham TH, et al, eds. Facts and Comparisons. St Louis, Missouri: Facts and Comparisons.
3. Coyle EA, Prince RA.Urinary Tract Infections and Prostatis. In: DiPiro JT, Talbbert RL, Yee GC, et al, eds. Pharmactherapy: A Pathophysioloigc Approch, Fifth Edition. New York. McGraw Hill, 2002. 1981-1996.
4. Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America. Clin Infect Dis 1999; 29:745-758.
5. Red Book Update, Montvale, NJ; February 2003.

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